



**DEPARTMENT OF VETERANS AFFAIRS
Veterans Health Administration
Washington DC 20420**

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In Reply Refer To: 111

September 22, 2009

UNDER SECRETARY FOR HEALTH'S INFORMATION LETTER

OSTEOPOROSIS IN MEN

1. Purpose. The Veterans Health Administration (VHA) Patient Care Services Technical Advisory Program (TAP) has recently conducted a systematic review of screening, diagnosis, evaluation, and treatment of osteoporosis in men. This information letter reviews the salient points of the report and makes field recommendations.

2. Background

a. Osteoporosis is a major risk factor for low-trauma fractures, with minimal trauma defined as a fall from a standing position. In men, such fractures occur at about half the rate as women. However, in the aging male population the incidence of fracture is projected to increase markedly. In addition, after hip fracture, men are twice as likely as women to die, and more men than women lose independence should they survive hip fracture. While there have been no evidence-based guidelines on management of osteoporosis in men, there is a growing body of medical literature on methods for screening and treatment. Thus, a review of the evidence was performed to determine who should be screened, how it should be done, who should be evaluated further, and which treatments are likely to help men diagnosed with osteoporosis.

b. Men older than 50 years with several underlying conditions are potential candidates for osteoporosis screening. Examples are those men on oral glucocorticoid therapy, those who have already suffered a low-trauma fracture, men treated with androgen deprivation therapy (ADT) for prostate cancer, and men with malabsorption or alcohol abuse. Men with these risk factors need to be evaluated by history and physical examination and considered for bone density testing. Bone density is measured by dual energy x-ray absorptiometry (DXA), and available at many VA medical centers. As shown in the accompanying algorithm (see Attachment C), men found to have low bone density by DXA are candidates for treatment with calcium, vitamin D, and in some cases oral bisphosphonates or teriparatide.

3. Recommendations

a. It is recommended that the algorithm in Attachment C be used as a guide to choosing which men should be screened for osteoporosis using DXA. Men who have osteoporosis by DXA (a T-score* in the spine or hip of -2.5 or lower) need to be evaluated with history, physical examination, and a small number of laboratory tests, as listed in the algorithm (Attachment C). As shown on the algorithm, men with low bone mass (T-score between -1 and -2.4) also need evaluation and treatment. While there is some evidence that certain laboratory tests are worthwhile in women, at this time, the basis for the choice of laboratory tests in men is expert opinion.

b. For men who have osteoporosis or low bone mass, lifestyle recommendations include home safety measures to prevent falls, weight bearing exercise, and enriching diet or using supplements to increase calcium and vitamin D intake. In addition, of several treatments for osteoporosis in men, the bisphosphonates oral alendronate, oral risedronate, and intravenous zoledronic acid are Food and Drug Administration (FDA)-approved for treatment in men to increase bone mineral density in those with the lowest bone density measurements in randomized, controlled trials. Other potential treatments are nasal calcitonin and teriparatide, part of the parathyroid hormone molecule. For patients with underlying disorders that cause low bone mass, such as hypogonadism, treatment of the underlying disorder is generally recommended. Finally, for patients with complicated problems or management difficulties, referral to an osteoporosis specialist is recommended. Most VA medical centers will have an endocrinologist, rheumatologist, geriatrician, or internist identified as an expert in osteoporosis.

4. References

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** The "T-score" is the bone density compared with what is normally expected in a healthy adult male or female. The "T-score" is the number of standard deviations above or below the standard.*

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5. Inquiries. The Office of Patient Care Services (11), Medical-Surgical Services (111) is responsible for the contents of this Information Letter. Questions regarding this information may be addressed to the National Program Director of Endocrinology and Diabetes at (973) 676-1000 x1693 or the Chief of Endocrinology and Metabolism at (804) 675-5424.

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ATTACHMENT A

BRIEF EXPLANATION OF THE ALGORITHM

1. The screening portion of the algorithm uses case findings for those men older than 50 years with specific risk factors for osteoporosis (e.g., previous fracture, oral glucocorticoid therapy, and androgen deprivation therapy (ADT) for prostate cancer). These are the men who need to be screened first.
2. For those men who have osteoporosis by dual energy x-ray absorptiometry (DXA) (T-score of -2.5 or worse in spine or hip [or forearm if spine cannot be interpreted]), a clinical evaluation is needed. In addition to history and physical exam, a few laboratory tests are indicated, including 25-hydroxyvitamin D level, serum calcium, serum albumin, serum creatinine, urinary calcium and creatinine (preferably a 24-hour specimen), and consideration of parathyroid hormone, phosphate, thyroid stimulating hormone (TSH), total testosterone, and alkaline phosphatase levels. A complete blood count (CBC) and serum proteins may provide a clue to multiple myeloma, which can look similar to osteoporosis on a spine x-ray. If there is evidence of a secondary cause of osteoporosis, it needs to be treated, or the patient needs to be referred to an osteoporosis specialist. Many of these patients still need treatment for osteoporosis.
3. For those patients who have low bone mass (osteopenia = T-scores* between -1 and -2.5), it is necessary to use clinical judgment. In the bisphosphonate clinical trials, some men had T-scores between -2 and -2.5 and they responded to therapy. In addition, the patient with important secondary causes such as oral glucocorticoid therapy or ADT usually needs evaluation and treatment or referral to a specialist. If the patient has suffered a low trauma fracture as an adult, evaluation and treatment are definitely indicated. For those patients at lower risk, lifestyle counseling (adequate calcium, vitamin D, muscle-building exercise, fall risk reduction) are recommended, with consideration of a re-evaluation, possibly including a repeat DXA, in 2 years.
4. Treatment for osteoporosis includes all of the lifestyle counseling mentioned previously, but it is important to be sure that vitamin D is adequately replaced. For most men, oral alendronate and risedronate and intravenous zoledronic acid have been Food and Drug Administration (FDA)-approved to increase bone mineral density in men. There have been no studies large enough to demonstrate that bisphosphonates decrease clinical fracture risks in men, but the effects on surrogates for fracture (bone density and bone turnover markers) are the same in men and women. If the patient has side effects or at 2 years appears not to have responded (by DXA), then referral to the osteoporosis specialist is indicated. For most patients, even after referral, the primary clinician should be able to manage the long term treatment of men with osteoporosis. From studies in women, at least 5 years of bisphosphonate treatment are necessary.

ATTACHMENT B

FREQUENTLY ASKED QUESTIONS (FAQS)

1. How common is osteoporosis in the male Veteran population?

It is estimated, from screening studies, that osteoporosis is very common. If defined by dual energy x-ray absorptiometry (DXA) of spine and hip only, there are at least 600,000 Veterans in Veterans Health Administration (VHA) health system who have osteoporosis. If the forearm bone density is measured, the number is more than 900,000, almost 14 percent of all male Veterans cared for by VHA. **NOTE:** *The specific indications for DXA testing, such as glucocorticoid or androgen deprivation therapy (ADT), prior fracture, and alcohol abuse are common among Veteran patients.*

2. How were the indications for screening selected?

Indications for screening were based on the World Health Organization (WHO) risk factors for osteoporosis, an evidence synthesis of the osteoporosis literature, plus reviews of osteoporosis in men. The indications listed are those for which the evidence is strongest. There may be other men who should be considered for evaluation on an individual basis. Examples of potential indications might include current smoking in the elderly, rheumatoid arthritis, organ transplantation, and mobility disorders. As more information becomes available, other indications for screening may be recommended.

3. Why was DXA of the spine and hip selected as the only valid tests for measurement of bone density?

While hip bone density predicts hip fracture better than DXA measurement at any other site, spine bone density also predicts fracture and may identify other men at risk. This may be particularly true for middle-aged men, who usually present with vertebral fracture or osteopenia on x-ray. For patients in whom the spine DXA cannot be interpreted (usually due to osteophytes and other arthritic changes of the spine), a forearm DXA is recommended.

4. How were the T-score cut-offs selected?

In general osteoporosis has been diagnosed in patients with DXA T-scores of -2.5 or worse. Yet in absolute numbers, more patients who fracture have a T-score between -1.0 and -2.4, called osteopenia or low bone mass. The reason for this is simply that there are so many more men who have DXA measurements in the osteopenic range. Nonetheless, fracture risk is highest for those with the lowest T-scores. For those men with spine or hip T-scores of -2.5 or worse, treatment is indicated. In the randomized controlled trials of treatment for men with low bone mass, the various agents tested also decreased the fracture risk in men with T-scores between -2 and -2.5. Thus, because anti-osteoporosis drugs work in such men, these men can also be considered for treatment.

5. *How were the basic laboratory tests selected?* ++

Based on studies in women and on expert opinion, the basic laboratory tests were chosen for the following reasons: serum 25-OHD is the best circulating reflection of the patient's vitamin D status, and many men have low levels, contributing to osteoporosis. Treatment is easy and inexpensive. The serum calcium (and consideration of phosphate and PTH) was chosen because hyperparathyroidism may lead to bone loss and hypocalcemia may be seen in patients with malabsorption. The serum albumin is used to correct the serum calcium: adjust calcium upwards by 0.8 milligram per deciliter (mg/d) for every 1 gram per deciliter (gm/dL) decrease in the serum albumin. Hyperthyroidism may lead to osteoporosis as can hypogonadism. Thus, the serum TSH is a good screening test for hyperthyroidism, and the serum total testosterone (perhaps with gonadotropins LH and FSH) can be used to exclude hypogonadism. If these conditions are present, then evaluation of the underlying disorder should precede that of the low bone mass. The complete blood count (CBC) and serum proteins may provide hints that the patient has multiple myeloma, which can lead to changes on spine x-ray that mimic osteoporotic fracture. Suspicion of multiple myeloma should lead to immediate evaluation.

6. *Provide a rationale for the management of male Veterans with a T-score* between -2.4 and -1.*

For those male Veterans who has a T-score worse than -1.0 but better than -2.5, other factors must be present before evaluation of bone disease; and treatments to prevent fracture are warranted. If the male Veteran has chronic (greater than 3months) exposure to oral glucocorticoids, the fracture risk is high and guidelines recommend evaluation and treatment. For the male Veteran who is undergoing androgen deprivation therapy for prostate cancer, pharmacologic prevention of osteoporosis or a repeat DXA within a year can be considered. Most experts would recommend pharmacologic therapy for those men who have had a low trauma fracture (defined as a fracture due to a fall from a standing position). For those male Veterans who do not have these risk factors, patients need to be counseled regarding increasing dietary or supplemental calcium, vitamin D supplements, weight bearing exercise, and home safety and fall risk reduction.

7. *What are the non-pharmacologic interventions to reduce fracture risk?*

There is modest evidence that calcium and vitamin D has a small salutary effect on bone mineral density. Weight bearing exercise can improve lower body strength and to a small extent bone density. There is some evidence that vitamin D treatment and exercise may decrease fracture risk. In some studies, hip protectors have decreased fracture risk, but other studies have failed to confirm efficacy. Fall risk reduction by improving home safety and improving balance and lower body strength will likely lead to decreased fractures.

++ *Tests: 25-OHD = 25 hydroxy vitamin D; PTH = parathyroid hormone; TSH = Thyroid Stimulating Hormone; LH = Luteinizing hormone; and FSH = Follicle Stimulatory Hormone.*

8. *Why are only bisphosphonates recommended as treatment?*

Secondary causes of osteoporosis, if diagnosed, needs to be treated first. In primary and secondary osteoporosis, several studies demonstrate the efficacy and general safety of bisphosphonates in men. Alendronate, risedronate, and zoledronic acid are FDA-approved in men, to increase bone mineral density and decrease vertebral fractures found on spine x-ray. In addition, there is one small study showing that men with strokes have fewer hip fractures if treated with risedronate. Although bisphosphonates decrease clinical fractures in women, there are no studies large enough to demonstrate decreased clinical fractures in men. Nasal calcitonin increases bone mineral density in women, but there are no studies in men. Teriparatide increases bone mineral density markedly in men and decreases vertebral fractures seen on x-ray. For some men, this may be appropriate therapy. However, teriparatide must be administered by daily injection, and it is expensive. For this reason, patients who might be candidates for teriparatide need to be referred to an osteoporosis expert. For hypogonadal men, testosterone replacement improves bone mineral density, but there are no fracture studies. For those patients who have had a hip fracture, intravenous zoledronic acid has been shown to decrease subsequent fractures and mortality.

9. *How were the Vitamin D and calcium dosages determined for the prevention and treatment of male osteoporosis?*

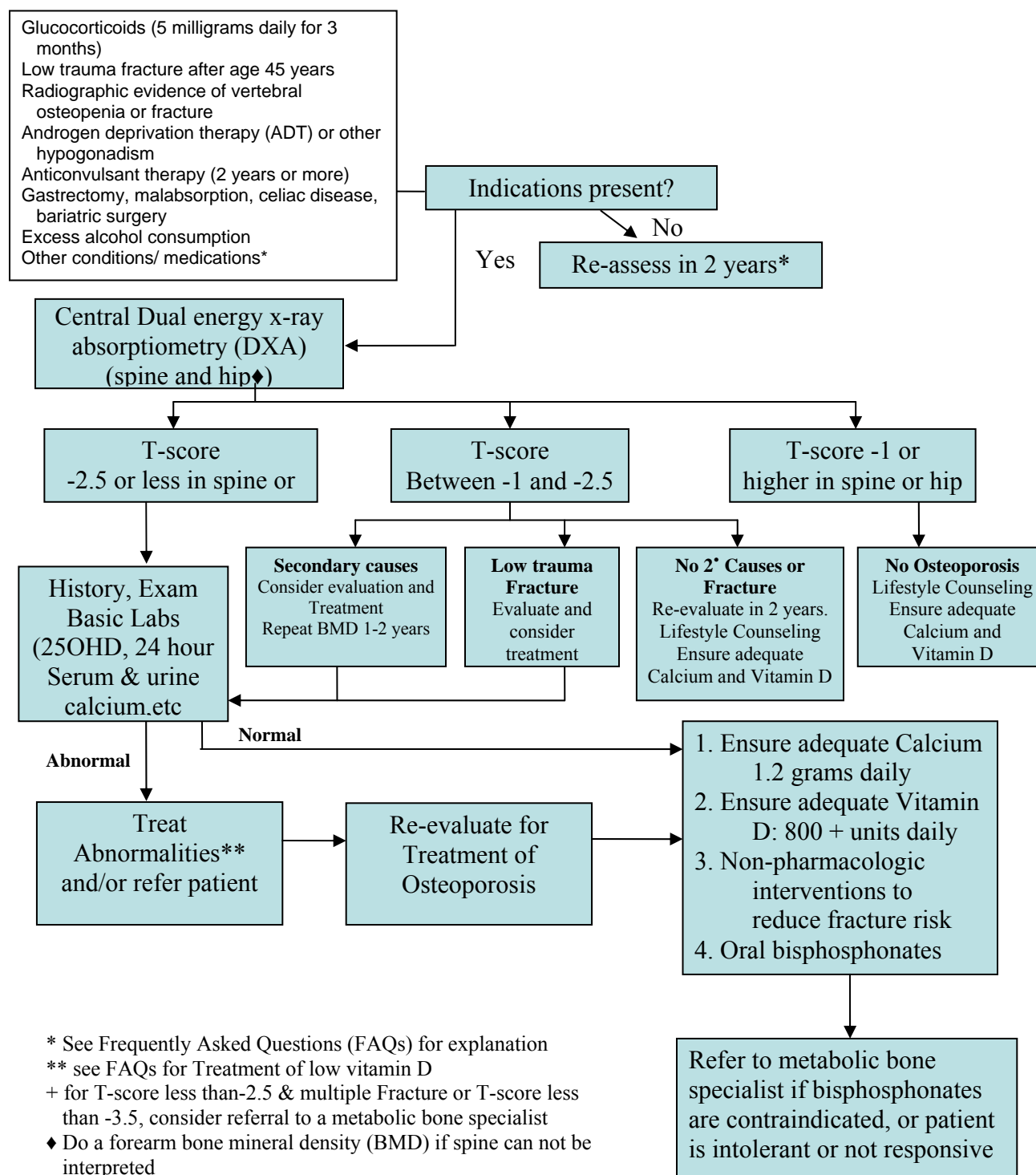
The general recommendations for adults are 1200 mg of calcium daily and at least 800 units of vitamin D daily. For many men, more than 800 units daily will be necessary to restore the 25-hydroxyvitamin D level to the normal range.

10. *Who is a metabolic bone specialist?*

There is no one discipline that defines a metabolic bone disease specialist. Subspecialists in Endocrinology, Rheumatology, or Geriatrics often have expertise in this area. However, there may be internists who have developed osteoporosis expertise. Physicians who can act as local osteoporosis experts need to be identified at each VA medical center.

ATTACHMENT C

SCREENING, DIAGNOSIS, EVALUATION, AND TREATMENT OF MALE OSTEOPOROSIS



ATTACHMENT D

ABBREVIATIONS USED

1. DXA	Dual energy x-ray absorptiometry
2. ADT	Androgen deprivation therapy for prostate cancer
3. OST	Osteoporosis Self-Assessment Tool (based on age and weight)
4. T-score	Number of standard deviations from normal men
5. BMD	Bone mineral density
6. GC	Glucocorticoid

Laboratory Tests:

7. 25OHD	25-hydroxyvitamin D (<i>measure of vitamin D status</i>)
8. U Ca/Cr	Urinary calcium and creatinine
9. PTH	Parathyroid hormone
10. PO4	Serum phosphate
11. TSH	Thyroid stimulating hormone
12. CBC	Complete blood count
13. AP	Alkaline phosphatase